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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,444	REID ET AL.	
	Examiner	Art Unit	
	MARIA LEAVITT	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-7,9-15 and 17-20* is/are pending in the application.

4a) Of the above claim(s) *6 and 12* is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,4,5,9-11 and 13* is/are allowed.

6)☒ Claim(s) *14,15 and 17-20* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Applicant's amendment filed on 07-29-2008 has been entered.
3. Status of claims. Claims 1, 2, 4-7, 9-15 and 17-20 are currently pending. Claims 1, 4, 9, 10, 13, 14, and 20 have been amended by Applicant's amendment filed on 07-29-2008. Claims 6 and 12 were previously withdrawn from consideration as being directed to a non-elected species pursuant to 37 CFR1.14 (b), there being no allowable generic or linking claim. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
4. The examiner acknowledges Applicants' submission of references as Exhibits A-R at pages 11 to 154 of Applicants' Remarks filed on 07-28-2008.
5. The examiner also acknowledges that an error was inadvertently made in the objection of claim 17 under 37 CFR 1.121(c), as no claims' amendment was filed on 12-18-2007 for the instant application. The examiner appreciates the correction.
6. Therefore, claims 1, 2, 4, 5, 7, 9-11, 13-15 and 17-20 are currently under examination to which the following grounds of rejection are applicable.

Response to Applicant's Remarks

Withdrawn objections/rejections in response to Applicant arguments or amendments.

Claim Objection

In view of Applicants' amendment of claims 1, 9, 13, 14 and 20 to delete the phrase "of at least", objection to claims 1, 9, 13, 14 and 20 has been withdrawn.

In view of Applicants' amendment of claims 4 and 10 to insert the phrase "comprising administering", objection to claims 4 and 10 has been withdrawn.

Rejections maintained in response to Applicant arguments or amendments.

Claim Rejections - 35 USC § 112- First paragraph- Scope of Enablement

Claims 14 and 19 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

> a method of inhibiting urogenital pathogens colonization of the urogenital tract in women comprising administering a therapeutically effective amount of *Lactobacillus iners* and a pharmaceutically acceptable carrier, wherein said *Lactobacillus iners* is administered orally or vaginally,

does not reasonably provide enablement for a method for reducing the risk of bacterial vaginosis and bacterial vaginosis pathogens as recited in claim 14 or the method for treating **any infection** in a subject as broadly embraced by claim 19.

Response to Applicants' arguments as they relate to rejection of claims 14 and 19 under 35 U.S.C. 112, first paragraph.

At pages 6-10 of Remarks, Applicants argue that "since the filing date of present application, references in the art have confirmed that Lactobacillus can be administered to the vagina by the oral route". Moreover, Applicants cite the disclosure of Nishijima et al., (Exhibit

O) as "verification for a method of treating an infection, irrespective of the type of infection, and for maintaining a healthy urogenital flora. The reference also confirms the viability of application of the claimed method to pregnant female subjects". Furthermore, Applicants allege that "in view of the specification and well known knowledge in the art, one skilled in the art can make and use the appropriate lactobacilli in the methods as claimed in the present application, without undue experimentation. In view of the foregoing argument and the amendment to the claims, the rejection of Claims 14, 15 and 17- 20 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enabling support, is overcome". Such is not persuasive.

While applicants' amendment partially overcomes some of the enabling issues related to specific routes of administration, some additional issues remain that are discussed below. At the outset, the examiner notes that the effective filing date of the present application is **March, 28, 2002.** The following post filing publications have been submitted by Applicants:

Exhibit A. 2005, *Clin. Nutr.* pp. 481-91).
Exhibit B. 2007, *Pediatr Nephrol.* pp. 1315-20
Exhibit C. 2008, *J Urol.* pp. 485-90
Exhibit D. 2008, *Mol Sys Biol.* p. 157
Exhibit E. 2008, *APMIS,* pp. 263-77
Exhibit F. 2007, *Clic and Exp Immun.* pp. 470-479
Exhibit G. 2008, *J. Clin Gastroenterol.* pp. 1-5
Exhibit H. 2006, *Thorax.* pp. 611-5
Exhibit I 2008, *Mini Rev Med Chem.* pp 455-71
Exhibit J. 2005, *N Engl J Med* 1899-911
Exhibit K.2008, *Microbes. Infect.* pp. 620-627
Exhibit L. 2007, FAO Technical meeting on Prebiotics.
Exhibit M. 2007, *Obstet and Gynecol.* pp. 114-20
Exhibit N. 2005 ; *J Infect Dis.* pp. 394-8, Abstract.
Exhibit O. 2005, *J Clin Gastroenterol.* pp. 447-448
Exhibit P. 2006, *Microbes. Infect.* pp. 1450-4, Abstract
Exhibit Q. 2006, *Microbes Infect.* pp. 2772-6, Abstract.
Exhibit R. 2005, *Can J Microbiol.* pp. 777-81

The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. > Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004) ("a patent document cannot enable technology that arises after the date of application"). Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing. In re Gunn, 537 F.2d 1123, 1128, 190 USPQ 402,405-06 (CCPA 1976); In re Budnick, 537 F.2d 535, 538, 190 USPQ 422, 424 (CCPA 1976) (In general, if an applicant seeks to use a patent to prove the state of the art for the purpose of the enablement requirement, the patent must have an issue date earlier than the effective filing date of the application.). While a later dated publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling, applicant can offer the testimony of an expert based on the publication as evidence of the level of skill in the art at the time the application was filed. Gould v. Quigg, 822 F.2d 1074, 1077, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987). [emphasis added]

Though post filing art teaches, for example, that that probiotic prophylaxis is effective as antibiotics prophylaxis in children with persistent primary vesicoureteral reflux (Exhibit B), intravesical instillation of epirubicin plus oral administration of *L. casei* as a promising treatment for preventing recurrence after transurethral resection for superficial bladder cancer (Exhibit C), probiotic yogurt intake was associated with significant anti-inflammatory effects that paralleled the expansion of peripheral pool of putative Treg cells in inflammatory bowel disease patients (Exhibit F), supplementation of conventional yogurt with *lactobacilli* species *L. rhamnosus GR-1*

and L. reuteri RC-14 contribute to increase CD4 count in 11/12 HIV/AIDS treated patients in relation to 3/12 in the control (Exhibit G) and others, there is not factual evidence supporting that orally administered *L. iners* would provide a beneficial treatment of respiratory and urinary track infections, let alone any infection in a subject as broadly encompassed by claim 19. Furthermore, Applicants submitted references do not show what one skilled in the art knew at the effective filing date of the present application. Indeed, the delivery of *L. iners* in any form as a probiotic to prevent and/or treat urogenital infection has not previously been disclosed in the state of the art at the time of filing. At best, Falsen et al., teaches the discovery of a new species of the genus Lactobacillus: Lactobacillus iners, isolated from human clinical specimens of the vagina (International Journal of Systematic Bacteriology, 1999, 217-221). However, this disclosure would have not provided sufficient guidance to consider *L. iners* for oral or vaginal probiotic applications, particularly after the unpredictably of the art at the time of filing further illustrated by the use of recombinant *L. iner* merely as deliver vehicle and not as a probiotic strain to treat gastro intestinal track disorders (see Hans et al., particularly, col. 3, line 24, Hans et al., WO01/02570, Publication date Jan. 11, 2001. Citations are from the National Stage U.S. Patent No. 7,220,418. The National Stage is deemed an English language translation of the PCT). Post filing art further confirms the unpredictability in relation to prevalence of distinct *lactobacilli* species in bacterial vaginosis as evidence by Ferri et al., 2007 (Clin Microbiol. pp. 1016–1018). The author states:

> *"L. iners* is rare in grade Ia specimens; however, it is prevalent in grade Ib, a variant of normal, and in grade III, representing BV. The "protective" role of individual vaginal *Lactobacillus* species is unclear. We speculate that *L. iners* is a transitional species and that an *L. crispatus*-predominant species composition represents a stable normal flora" (p. 1018, col. 1, paragraph 2).

In particular, in relation to Exhibit G, which confirmed that probiotic *lactobacilli* could boost the CD4 count in HIV/AIDS patients, the examiner discussed, at page 8 in the previous office action filed 04-29-2008, that these results are not predictive of all species of *lactobacilli* as each species is genetically distinct resulting in different physiological functionalities For example, *L. reuteri* produce bacteriocins called reuterin (Talarico and Dobrogosz, Antimicrob Agents Chemother pp. 674-9, 1989), whereas *L. rhamnosus* do not. Similarly, *L. reuteri* RC-14 produce low amounts of hydrogen peroxide, whereas *L. crispatus 33820* produce high amounts *and L. rhamnosus GR-1* do not produce at all *(*Saunders et al., 2007, Colloids Surf B Biointerfaces, Abstract). Likewise, just because one *E. coli* strain causes urinary tract infection, does not mean that the same strain causes diarrhea. On the contrary, there is no such overlap - strains are uropathogenic, or enterotoxigenic, or some are even avirulent and beneficial to the host (Mims et al., Medical Microbiology, 2004, pp. 280-284).

As discussed above, and for the reasons of record, the disclosure provided by the applicant is not fully enabled for the scope embraced by the claims because applicant does not provide sufficient guidance to make and use a method for reducing the risk of bacterial vaginosis and bacterial vaginosis pathogens and a method for treating **any infection** in a subject as broadly embraced and set forth by the invention in light of the guidance provided in the specification and knowledge available to one of ordinary skill in the art at time of filing.

Claim Rejections - 35 USC § 102

Claim 15 is drawn to a pharmaceutical composition comprising *L. iners* and a pharmaceutically acceptable carrier. The as-filed specification defines a "pharmaceutically-

acceptable carrier" as any one or more compatible solid or liquid able of being commingled without substantially decreasing the pharmaceutical efficacy of the composition (p. 11). Thus the pharmaceutical composition can be broadly interpreted as any media that comprises *L. iners* without affecting the efficacy of the composition.

Claim 15 remains rejected under 35 U.S.C. 102(b) as being anticipated by Falsen et al., Journal of Systematic Bacteriology, 1999, 217-221.

Falsen et al., teaches a new isolated species of Lactobacillus: *L. inners* that growths in an agar culture supplemented with 5% horse blood at 37C in air plus CO_2. Clearly, Falsen et al., discloses a prebiotic nutrient utilized by lactobacilli to stimulate and/or enhance growth of lactobacilli relative to pathogenic bacteria, e.g., serum, and a pharmaceutically acceptable carrier, e.g., water. Thus by teaching all the limitations of claim 15, Falsen et al., anticipates the instant invention.

Response to Applicants' arguments as they relate to rejection of claim 15 under 35 USC § 102.

At page 11 of Remarks, Applicants allege that "Falsen et al. simply identify a single *L. iners* organism, which identification by itself, without more, does not teach or suggest that the *L. iners* organism can be placed in a pharmaceutical or food carrier and delivered for therapeutic purposes". Moreover, Applicants argue that "the agar media used by Falsen et al. is welI well known to be capable of growing many types of microorganisms including pathogenic ones. In this regard, Applicants respectfully submit that contrary to the Examiner's allegation that a prebiotic broadly encompasses any growth media that enhances the growth of the bacteria, a prebiotic recited by Claim 15 is clearly defined by the present application as "a... substrate that..,

selectively enhances the growth and/or the metabolic activity of a bacterium or a group of bacteria. A prebiotic also includes a nutrient utilized by lactobacilli or bifidobacteria to stimulate and/or enhance growth of lactobacilli or bifidobacteria relative to pathogenic bacteria." See page 7, lines 5-9 of the specification (emphasis added). Thus, Falsen et al. do not teach or suggest that blood agar can be a prebiotic". Such is not persuasive.

As discussed in the previous office action filed on 04-29-2008, the culture medium of Columbia Agar Base comprises, for example, carbohydrates e.g., corn starch for *L. iners* growth (See, BBL, Columbia Agar, Difco). Applicants have not submitted evidence that the new isolated species of *L. iner* could not grow and proliferate in an agar culture media enriched with 5% horse serum blood as demonstrated by the successful growth in this culture media of *L. iner* taught by Falsen et al.

At page 11 of Remarks, Applicants "submit additional evidence to demonstrate that blood is not a prebiotic (the definition of which can be found in "Food component that confer a health benefit on the host through modulation of the microbiota" - Food Quality and Standards Service (AGNS) Food and Agriculture Organization of the United Nations (FAO) September i5-16, 2007) (Exhibit L)". As such applicants allege that Falsen does not anticipate claim 15. Such is not persuasive.

The Columbia agar (Difco) used to grow *L. iner* taught by Falsen et al. is not necessarily blood as Applicants contend. The examiner refers Applicants to the identified components present in the Columbia agar (Difco) medium (See, BBL, Columbia Agar, Difco) . Moreover, Applicants have not pointed out where in Exhibit L there is evidence that the culture medium of Columbia Agar Base does not selectively stimulate the growth and/or activity of *L. iner.*

Claim Rejections - 35 USC § 112- First paragraph- New Matter

Claim 20 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Response to Applicants' arguments as they relate to rejection of claim 20 under 35 USC § 112- First paragraph- New Matter

At page 4 of Remarks Applicants argue that "the present invention is partly predicated upon the recognition that *L. iners'* ability to restore and maintain health of the urogenital tract begins with its ability to reduce the infectious agents which originate in the intestine and ascend from the rectum to the vagina. Neither HIV nor herpes simplex virus infects in this manner". In addition, Applicants contend that "the present invention recognizes that bacterial vaginosis organisms and the condition itself were displaced coinciding with the presence of *L. iners*. Since bacterial vaginosis has a prevalence of 29% (Allsworth and Peipert, "Prevalence of bacterial vaginosis: 2001-2004 National Health and Nutrition Examination Survey data." Obstet Gyn ecol. 2007 Jan; 109(1): I 14- 20) (Exhibit M), the recognition of *L. iners* in healthy subjects by the present invention proves that *L. iners* has anti-infective properties. Thus, Applicants submit that the present inventors had possession of the subject matter at the time of the present application was filed [emphasis added]. Such is not persuasive.

Claim 20 has been amended to insert the phrase, "wherein vaginal pathogens are gastrointestinal or urogenital bacterial flora". The specification as filed does not provide a close

definition of the phrase "endogenous pathogen" but merely discloses that at page 7, last paragraph, "the Lactobacillus iners of the present invention will **inhibit growth and/or adhesion of enteric pathogens to gastrointestinal surfaces**", and at page 13, paragraphs 2 and 3, "The introduction or administration of lactobacilli probiotics to the intestine and passage onto the urogenital tract, and their subsequent production of anti-pathogenic products (e.g., biosurfactants, acids, hydrogen peroxide, bacteriocins) modulates the immune response against infection and disease and reduces the risk of medical device associated infections", as such, and in view of the customary and ordinary meaning of the term "enteric" in the art as "relating to, or affecting the intestines " (Webster's Seventh New Collegiate Dictionary, G. C. Merriam Co.), the phrase "will **inhibit growth and/or adhesion of enteric pathogens to gastrointestinal surfaces**" does not provide sufficient guidance for inhibiting or displacing indigenous-endogenous **vaginal pathogens** that **are gastrointestinal or urogenital bacterial flora**. Thus the breadth of claim 20 is broader than the guidance provided in the specification. **Additionally, it is unclear whether "displacing vaginal pathogens" refers to inhibiting binding or adhesion of other vaginal endogenous pathogens or competing with pathogens already bound to the vaginal mucosa to unbind them.** The examiner notes that the purpose of the written description requirement is "to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." In reEdwards, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978). Hence, the post-filing art of Allsworth and Peipert. 2007, Obstet Gyn ecol. 2007 Jan; 109(1): I 14- 20) (Exhibit M) does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of the filing of the application,

New grounds of objection

Claims objection

Claim 7 is objected to because of the following informality. Claim 7 which depends on claim 4 recites "the probiotic organism". In addition, claim 1 has been amended to recite "a first probiotic Lactobacillus iners". Claim 4 depends on claim 1. Claim 4 only refers to "a second probiotic organism". Thus there is it unclear whether claim 7 refers to the first or the second probiotic. The insertion of the phrase "the second probiotic" will help to clarify the meaning of claim 7.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that they fail to point out what is included or excluded by the claim language.

Claims 17 and 18 which depend on claim 15 recite "The method of any of Claims 7 or 15". However, claim 15 only refers to "a pharmaceutical composition". Thus there is not a proper antecedent bases for said method in claim 15. As such, the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 103

The as-filed specification defines a "pharmaceutically-acceptable carrier" as any one or more compatible solid or liquid able of being commingled without substantially decreasing the pharmaceutical efficacy of the composition (p. 11). The specification as filed defines a prebiotic

as "a prebiotic also includes a nutrient utilized by lactobacilli or bifidobacteria to stimulate and/or enhance growth of lactobacilli or bifidobacteria relative to pathogenic bacteria." (p. 5, paragraph 1).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims **15 and 16, 17** are rejected under 35 U.S.C. 103(a) as being unpatentable over Falsen et al., Journal of Systematic Bacteriology, 1999, 217-221, in view of BBL, Columbia Agar, Difco (of record) and Cavaliere (US Patent 6,277,370) and further in view of Gibson et al., (Gastroenterology, 1995, pp. 975-892).

Falsen et al., teaches a new isolated species of Lactobacillus: *L. inners* that grows in an agar culture (Difco ™ Columbia Agar) supplemented with 5% horse blood at 37C in air plus CO_2. Clearly, Falsen et al., discloses a prebiotic nutrient utilized by lactobacilli to stimulate and/or enhance growth of lactobacilli relative to pathogenic bacteria, e.g., serum, and a pharmaceutically acceptable carrier, e.g., water.

Falsen et al., does not specifically disclose that *L. inners* is beneficial to health nor the components of the Difco ™ Columbia Agar culture medium.

However, at the time the invention was made, Cavaliere discloses a pharmaceutical composition comprising of lactobacilli adapted for treatment of vaginosis and vaginitis, including *Lactobacillus brevis, Lactobacillus salivarius, Lactobacillus salivarius subs. salivarius, Lactobacillus jensenii, Lactobacillus catenaforme, Lactobacillus minutus* and others (col. 3, lines 19-27).

Moreover, at the time the invention was made, it was routine or well-established in the art to employ the culture medium of Columbia Agar Base comprising carbohydrates e.g., corn starch for incubation and bacterial growth (See, BBL, Columbia Agar, Difco).

Difco ™ Columbia Agar culture medium does not specifically comprise the carbohydrates inulin and oligofructose.

However, at the time the invention was made, Gibson discloses that carbohydrates, inulin and oligofructose, are beneficial stimulating the growth of species of Bifidobacterium, a genus of bacteria considered beneficial for health. Moreover, Gibson teaches that dietary addition of inulin or oligofructose alter the balance of colonic bacteria towards a healthier microflora (Abstract).

Thus in view of the benefits of using as carbohydrates inulin or oligofructose to selectively stimulate the growth of species of bacteria considered beneficial to health as disclosed by Gibson, it would have been *prima facie* obvious for the skilled artisan to modify the carbohydrate component of the Columbia Agar, Difco by replacing starch with inulin or oligofructose to improve the growth of *L. inners* in the course of routine optimization as it was well known in the art at the time of filing the beneficial association of lactobacilli and treatment of vaginosis. One of ordinary skill in the art would have had a reasonable expectation of success in making pharmaceutical composition comprising L. *inners,* a prebiotic and a pharmaceutical carrier, wherein the prebiotic is inulin or oligofructose, because Falsen et al., discloses growth of *L. inners* Difco ™ Columbia Agar culture medium comprising carbohydrates and because Gibson actually exemplify pharmaceutical

Conclusion

Claims 14, 15, 17-19 and 20 are rejected.

Claim 7 is objected.

Claims 1, 2, 4, 5, 9-11 and 13 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/Maria Leavitt/
Maria Leavitt, PhD
Examiner, Art Unit 1633